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FULL PAPER

Comparison of α-amylase, α-glucosidase and lipase inhibitory activity of different types of vinegar

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Abstract

Vinegar is regarded as a fine example of a traditional food that has several medicinal values. It is used as a home-remedy for the management of diabetes and obesity. We investigated how selected vinegar inhibit the digestive enzymes involved in carbohydrate and lipid metabolism. A total of seven types of vinegar were examined as follows: apple cider (ACV), balsamic (BV), brown rice (BRV), distilled white (DWV), malt (MV), nipah palm (NPV), and red wine (RWV) vinegar. In vitro enzyme inhibition tests were performed using α-amylase and lipase from porcine pancreas, and α-glucosidase from *Saccharomyces cerevisiae*. In the α-amylase assay, NPV (IC_{50} = 60.97±1.71 mg/mL) exhibited the strongest inhibitory effect, while RWV (IC_{50} =786.7±0.96 mg/mL) showed the lowest inhibitory effect. RWV (IC_{50} =92.49±1.51 mg/mL), by contrast, had the highest inhibitory effect against α-glucosidase and was followed by NPV (IC_{50} = 227.5±1.06 mg/mL) and BRV (IC_{50} = 565.1±2.65 mg/mL). All of the samples showed potent inhibitory effects against pancreatic lipase, with MV having the strongest and ACV the lowest effects, respectively. IC_{50} values ranged from 48.45 mg/mL to 399.8 mg/mL. A concentration-dependent inhibitory effect was recorded for each of the vinegar against all three tested enzymes. None of the vinegar, however, exceeded the effects recorded for the standard drugs. Interestingly, a weak correlation was found between total acidity and enzyme inhibition, which asserted the presence of bioactive compounds in the vinegar. As a conclusion, vinegar can be incorporated into the diet to lower the meal's glycaemic index and benefit those at risk of diabetes as well as diabetics.

1. Introduction

Diabetes mellitus (DM) is a heterogenous metabolic disorder characterized by persistent hyperglycaemia in fasting and/or postprandial states (Sperling *et al*., 2014). The prevalence of DM is increasing at an alarming rate. According to the International Diabetes Federation, 9.3% of adults worldwide were living with DM in 2019, with Type 2 DM accounting for nearly 90% of the cases (IDF, 2019). Obesity has been strongly linked to Type 2 DM (Schnurr *et al*., 2020). Research has shown obese adults to be seven times more likely to developing Type 2 DM than adults with healthy weights (Abdullah *et al*., 2010). DM can be managed by controlling postprandial glucose levels and reducing body weight through the suppression of carbohydrate and lipid hydrolysing enzymes (Wasai *et al*., 2018). Pancreatic α-amylase and intestinal α-glucosidase are exo-acting glycoside hydrolases that are essential for the metabolism of carbohydrates (Feng *et al*., 2015). Suppression of these enzymes effectively ameliorates postprandial hyperglycaemia by limiting enteral carbohydrate absorption. Pancreatic lipase, on the other hand, is a key enzyme for dietary fat metabolism. It hydrolyses up to 70% of the total dietary fats ingested to create readily absorbed forms in the small intestines (Liu *et al*., 2020). It can be hypothesized that by inhibiting the activity of α-amylase, α-glucosidase and pancreatic lipase, the onset of Type 2 DM and its complications may be delayed. A considerable number of functional foods have been shown to be potent inhibitors of digestive enzymes (Kwon *et al*., 2008; Venkatakrishnan *et al*., 2019; Kan *et al*., 2020). Vinegar is a functional food that is widely consumed. Over the past decades, the therapeutic effects of many kinds of vinegar have been thoroughly examined (Samad *et al*., 2016). Numerous clinical studies have highlighted the role of vinegar in

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controlling blood glucose levels and normalizing the lipid profiles of diabetic patients (Liatis *et al*., 2010; Johnston *et al*., 2013; Petsiou *et al*., 2014). Preclinical animal studies have also reported the effects of different vinegar on metabolic parameters (Yusoff, Ahmad, Al Hindi *et al*., 2015; Seo *et al*., 2015; Yamashita, 2016). Despite the large number of studies demonstrating the therapeutic effects of various vinegar, the mechanisms underlying the antidiabetic and anti-obesity activities of most vinegar remain elusive. This study was designed to test whether vinegar affects carbohydrate- and/or lipid-hydrolyzing enzymes as this could partly explain the observed therapeutic effects. Tests assessed the effects of these kinds of vinegar on α-amylase, α-glucosidase and pancreatic lipase. The correlations between enzyme inhibition and the total acid content were reported for each of the seven types of vinegar used.

2. Materials and methods

2.1 Chemicals

Alpha-glucosidase, porcine α-amylase, and pancreatic lipase were purchased from Sigma Aldrich Chemical (St. Louis, MO, USA). Acarbose, sodium hydroxide, and starch were supplied by Sigma Life Science (Waltham, MA, USA). Orlistat was purchased from J and K Scientific Ltd. All the reagents used were of analytical grade.

2.2 Vinegar samples and sample preparation

Seven types of vinegar were obtained from local retailers as follows: Apple cider vinegar (ACV), balsamic vinegar (BV), brown rice vinegar (BR), distilled white vinegar (DW), malt vinegar (MV), nipa palm vinegar (NPV) and red wine vinegar (RWV). These stock vinegar solutions were classified into grain-vinegar and fruit-vinegar based on the raw materials used in their respective production processes (Table 1). Vinegar samples were freshly prepared every time by diluting the stock solution with distilled water. Enzyme inhibition assays were conducted using samples at concentrations ranging from 4000 to 125 mg/mL.

Table 1. Vinegar samples

Type of Vinegar	Content of vinegar (as per label)
Apple cider vinegar	Apple juice and water
Balsamic Vinegar	Concentrated grape must and sulphites
Brown Rice Vinegar	Organic brown rice, water and koji seed
Distilled White Vinegar	Distilled white vinegar and water
Malt Vinegar	Malted barley extract and water
Nipah Palm Vinegar	Nipah sap and water
Red Wine Vinegar	Red wine and water

2.3 pH and acetic acid measurement

The pH value of each vinegar was measured using a pH meter (Hanna HI221 pH) followed by titration (Bakir *et al*., 2017). To perform the measurement, 5 mL of vinegar mixed with 1% of phenolphthalein as the indicator; were titrated using 0.1 M of NaOH. Acidity values were presented as acetic aside equivalent percentages calculated using the following equation:

$$\text{Percentage of acetic acid (\%)} = \frac{V \times E \times 100}{M} \quad (1)$$

Where V is the volume used of the titrant (NaOH) in litres, E is the vinegar equivalent (determined to be 0.006005), and M is the amount of the titrated vinegar (5 mL).

2.4 α-amylase inhibitory activity

The α-amylase inhibitory activity of each sample was evaluated according to Safamansouri *et al*. (2014). A 20 mM sodium phosphate buffer solution (pH = 6.9) containing 6.7 mM sodium chloride; was used. A starch solution (1% w/v) was prepared by mixing 1 g of soluble potato starch in 1 mL of the buffer solution. The α-amylase solution (50 unit/1 mL) was prepared by adding 0.01 g of α-amylase to 10 mL of the buffer. A colour reagent solution was obtained by mixing 0.1 g of 3,5-dinitro salicylic acid, 2.99 g of sodium potassium tartrate, and 0.161 g of sodium hydroxide in 10 mL of the buffer solution. Next, 50 µL of the vinegar sample was mixed with 150 µL of the starch solution and 10 µL of the enzyme solution in a 96-well plate. The plate was incubated for 30 mins at 37°C. The reaction was terminated by adding 20 µL of the colour reagent. The plate was further incubated in boiling water for 20 min. After cooling down to room temperature, the absorbance value of the reaction mixture was measured at a wavelength of 570 nm using a microplate reader (Bio Tek). Acarbose (20-0.313 mg/mL), an α-amylase inhibitor, was used as a standard reference. Alpha-amylase inhibition was presented as a percentage as follows:

$$\% \text{ Inhibition} = 100 \times [(\Delta A_{control} - \Delta A_{sample})/\Delta A_{control} \quad (2)$$

Where $A_{control}$ is the absorbance value of the control solution, and A_{sample} is the absorbance value of the sample. The half-maximal inhibitory concentration (IC_{50}) values indicated the concentration required of an α-amylase inhibitor to inhibit 50% of the enzymatic activity.

2.5 α-glucosidase inhibitory activity

The α-glucosidase inhibition activity of each sample was evaluated as previously demonstrated by Yusoff, Yam, Beh *et al*. (2015). A 0.1 M phosphate buffer (pH =

6.9) was used as the working buffer in this experiment. A yeast α-glucosidase (0.5 U/mL) solution and a 5 mM p-nitrophenyl-α-D-glucopyranoside (pNPG) solution were prepared in the working buffer and acted as the enzyme and substrate solutions, respectively. To perform the measurements, 50 µL vinegar aliquots were mixed with 100 µL of the α-glucosidase enzymatic solution in a 96-well plate. After a 10-min incubation period at 37°C, each well was topped up with 50 µL of the pNPG solution. The plate was incubated for 5 min at 37°C. Alpha-glucosidase activity was determined by measuring the absorbance value of the 4-nitrophenol released from the pNPG solution at a wavelength of 405 nm. Acarbose (20-0.313 mg/mL), α-glucosidase inhibitor, served as a standard reference. Alpha-glucosidase inhibition was expressed as a percentage value calculated as follows:

$$\%\text{Inhibition} = 100 \times [(\Delta A_{control} - \Delta A_{sample})/\Delta A_{control}] \quad (3)$$

Where $A_{control}$ is the absorbance of the control solution, A_{sample} is the absorbance of the sample. IC_{50} values indicated the concentration required of an α-glucosidase inhibitor to inhibit 50% of the enzymatic activity.

2.6 Pancreatic lipase inhibitory activity

The porcine pancreatic Iipase (PPL) activity of each sample was measured as previously described by Jo *et al*. (2017). A PPL enzymatic stock solution (0.1 mg/mL) was prepared in a 0.1 M Tris-HCl buffer (pH = 8.0). A 10 mM *p*-nitrophenyl butyrate (*p*-NPB) solution in acetonitrile served as the substrate solution. In a 96-well plate, 5 µL vinegar samples at different concentrations were mixed with 90 µL of the enzyme solution and incubated for 10 mins at 37°C. Then, 5 µL of the *p*-NPB solution was added to the reaction mixture. After a 15-min incubation period, the lipase inhibitory activity was determined by measuring the absorbance value of the formed *p*-nitrophenol at a wavelength of 405 nm. The inhibitory activities of the vinegar against pancreatic lipase were expressed as the percentage of inhibition and IC_{50} values. The following formula was used:

$$\%\text{Inhibition} = 100 \times [(\Delta A_{control} - \Delta A_{sample})/\Delta A_{control}] \quad (4)$$

Where $A_{control}$ is the absorbance of the control, and A_{sample} is the absorbance of the sample. All samples were run in triplicate. Orlistat (10-3.13 mg/mL), an inhibitor of pancreatic lipase, was used as a standard reference.

2.7 Statistical analysis

The data were expressed as the mean±standard mean error (SEM). Statistical significance was determined using one-way analysis of variance (ANOVA) followed by Tukey HSD as a post-hoc test. P values below 0.05 indicated statistical significance. The data was analysed using the IBM® SPSS statistical software.

3. Results and discussion

3.1 pH and total acidity

Table 2 shows the values of the pH and total acidity of the vinegar samples. The samples had pH values ranging from 2.62 to 3.23. RWV had the lowest pH, while ACV had the highest. The percentages of acetic acid in the samples were between 2.30±0.01% and 5.17±0.01%, with NPV exhibiting the lowest acetic acid content, and RWV showing the highest reading. These findings are in agreement with Bakir *et al*. (2017) as they reported pH values of eighteen vinegar ranging from 2.8 and 3.7 and total acidity values between 0.7±0.1% and 5.02±0.03%. According to Bakir *et al*. (2017), the pH value and the total acid content of vinegar are crucial determinants of its antimicrobial activity. The findings did not show a significant correlation between pH level or the total acid content of vinegar and its enzyme inhibitory effect.

Table 2. pH and total acidity values

Type of Vinegar	pH	Acidity (%)
Apple cider vinegar	3.23	4.83±0.02
Balsamic Vinegar	3.2	3.06±0.06
Brown Rice Vinegar	2.82	4.09±0.01
Distilled White Vinegar	2.62	4.96±0.01
Malt Vinegar	2.93	4.80±0.01
Nipah Palm Vinegar	3.04	2.30±0.01
Red Wine Vinegar	2.62	5.17±0.01

3.2 Inhibitory effects of vinegar against carbohydrate-hydrolyzing enzymes

This assay assessed the α-amylase enzymatic inhibitory activity of the seven selected vinegar against acarbose. Table 3 shows the IC_{50} values obtained for each of the vinegar and acarbose. All of the vinegar inhibited α-amylase, with the IC_{50} values being in the range of 60.97±1.71 mg/mL and 786.7±0.96 mg/mL. NPV had the strongest inhibitory effect, while RWV showed the lowest. However, the effect of NPV was minimal compared with that of acarbose as the latter was greater by 16.8 folds. Yet, enzyme inhibition was found to increase with increasing vinegar concentration for each of the samples (Figure 1A).

Likewise, the α-glucosidase inhibitory activity of each vinegar was observed to be concentration-dependent (Figure 1B). RWV caused the greatest α-glucosidase inhibitory effect (IC_{50} = 92.49±1.51 mg/mL) among the vinegar used. This was followed by NPV (IC_{50} = 227.5±1.06 mg/mL) and BRV (IC_{50} = 565.1±2.65 mg/mL). The lowest α-glucosidase inhibition was observed with MV (IC_{50} = 2030±0.83 mg/mL). Considering that the IC_{50} value of acarbose was found to be 17.02±7.26 mg/mL, acarbose surpassed the inhibitory

Table 3. IC_{50} values for α-amylase, α-glucosidase and lipase assays of seven types of vinegar

Type of Vinegar	IC_{50} (mg/mL±SEM)[a]		
	α-amylase	α-glucosidase	Lipase
Apple Cider Vinegar	665±0.29	866.7±1.52	399.8±0.08
Balsamic Vinegar	262.7±2.22	784.5±1.50	138.5±0.08
Brown Rice Vinegar	192.7±0.03	565.1±2.65	105.9±0.06
Distilled White Vinegar	359±0.03	430±1.62	58.25±0.08
Malt Vinegar	187.4±0.06	2030±0.83	48.45±0.14
Nipah Palm Vinegar	60.97±1.71	227.5±1.06	83.11±0.17
Red Wine Vinegar	786.7±0.96	92.49±1.51	112.5±0.04
Reference	3.64±1.00[b]	17.02±7.26[b]	5.01±0.03[c]

[a]Standard error of the mean (n=3), [b]Acarbose, [c]Orlistat

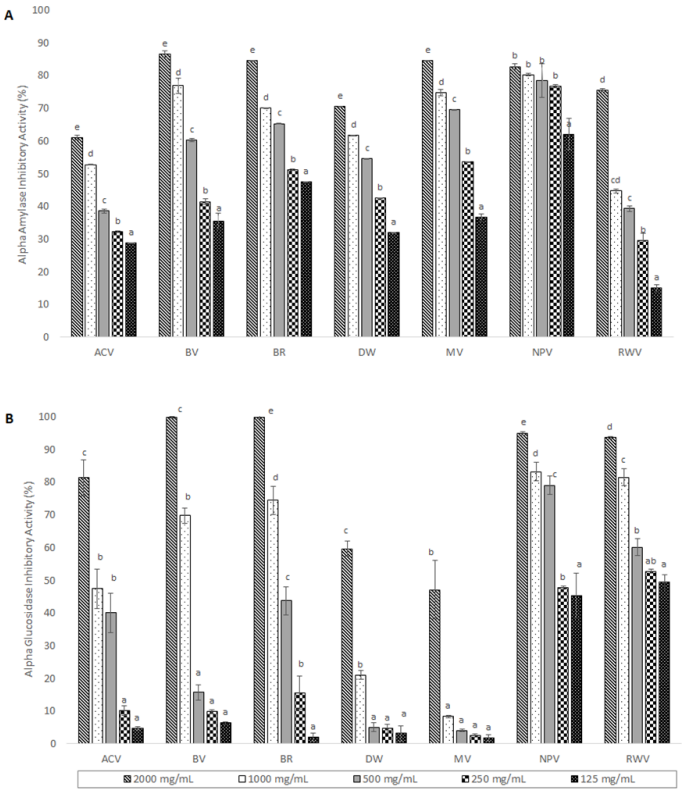

Figure 1. Dose dependent changes in percentage inhibitory activity of seven types of vinegar against **A**) α-amylase and **B**) α-glucosidase. Results are expressed as means±SEM for triplicates of each concentration. Different letters above error bars indicate significant differences ($p < 0.05$) among groups as analysed using Tukey's post-hoc test. ACV: apple cider vinegar, BV: balsamic vinegar, BR: brown rice vinegar: DW: distilled white vinegar, MV: malt vinegar, NPV: nipah palm vinegar, RV: red wine vinegar

effect of RWV by 5.4 folds. Both assays showed similar patterns of inhibition, except for red wine vinegar.

Overall, our data suggested that the vinegar tested possessed moderate inhibitory activities against carbohydrate-hydrolyzing enzymes. Similar findings were reported by Johnston *et al.* (2010) in healthy adults. The ingestion of two teaspoons of vinegar with a meal rich in complex carbohydrates was observed to reduce postprandial glucose levels by almost 20%. Our findings also agree with a report by Ogawa *et al.* (2000) which looked into the inhibitory effects of acetic acid, a major compound of vinegar, on dissacharidase activity in Caco-2 cells.

3.3 Pancreatic lipase inhibitory activity

All vinegar samples exerted moderate inhibitory effects against pancreatic lipase in a concentration-dependent manner (Figure 2). Table 3 shows the IC_{50} values of the vinegar samples to be in the range of 48.45 - 399.8 mg/mL. The samples inhibited lipase to varying extents as follows: MV > DWV > NPV > BRV > RWV > BV > ACV. The IC_{50} value of orlistat, the reference, was determined to be 5.01±0.03 mg/mL, which demonstrated that orlistat inhibited lipase by 9.7 folds as compared with MV, the most potent inhibitor among the tested samples. Pancreatic lipase is responsible for the digestion of dietary fat. Lipase inhibition due to vinegar intake may, thus, slow down the storage of fat and inhibit weight gain, which can be beneficial in terms of controlling obesity and delaying the onset of Type 2 DM (Dechakhamphu and Wongchum, 2015). Previous reports have highlighted the therapeutic effects of vinegar in obesity. Halima *et al.* (2016) showed that

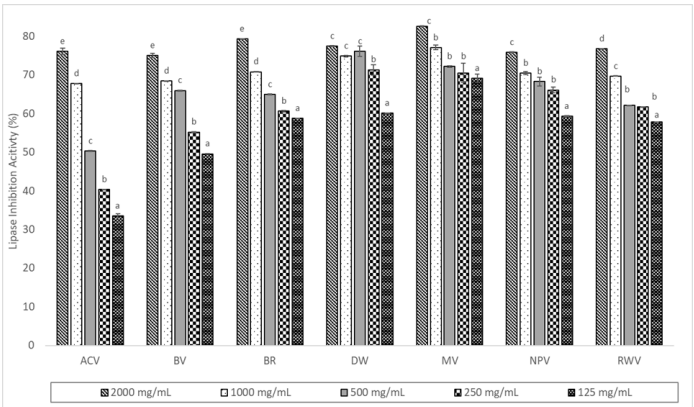

Figure 2. Dose dependent changes in percentage inhibitory activity of seven types of vinegar against lipase. Results are expressed as means±SEM for triplicates of each concentration. Different letters above error bars indicate significant differences ($p < 0.05$) among groups as analysed using Tukey's post-hoc test. ACV: apple cider vinegar, BV: balsamic vinegar, BR: brown rice vinegar: DW: distilled white vinegar, MV: malt vinegar, NPV: nipah palm vinegar, RV: red wine vinegar

treatment with apple cider vinegar significantly improved lipid homeostasis in diabetic rats by suppressing the activity of lipid-metabolizing enzymes. Additionally, Chen *et al*. (2012) and Chatatikun and Kwanhian (2020) respectively reported that Nipah palm vinegar and black vinegar powder attenuated the activity of pancreatic lipase.

3.4 Correlation of acetic acid content with α-amylase, α-glucosidase and lipase inhibitory effect

To determine whether enzymatic inhibition was subject to the acetic acid content of vinegar, a correlation analysis was performed (Figure 3). A negative correlation was observed between the acetic acid content and the α-amylase inhibitory activity of the samples. By contrast, positive correlations were observed between the acetic acid content, and α-glucosidase and lipase inhibitory activities, respectively. Overall, there was only a weak correlation between the acetic acid content of vinegar and its inhibitory activities against α-amylase, α-glucosidase and lipase (R^2 = 0.040, 0.101 and 0.356, respectively). The findings indicated possible inhibitory effects of some of the bioactive compounds present in the vinegar. Acetic acid is the major organic acid in vinegar, but other bioactive compounds have been documented in the past in different vinegar preparations. Those functional compounds include non-volatile organic acids, phenolic acids, and tetramethylpyrazine (TMP) (Xia *et al*., 2020). Work conducted on persimmon vinegar showed that citric acid and lactic acid worked with acetic acid to promote the appetite and stimulate the use of fatty acids (Moon *et al*., 2010). TMP was identified as a major compound in Chinese black vinegar, in which it exerted antioxidant and hypolipidemic effects (Chen *et al*., 2017). Phenolic acids, such as gallic acid, ferulic acid, caffeic acid and salicylic acid; have been identified in both grain- and fruit-vinegar, and have been shown to have promising antioxidant (Kelebek *et al*., 2017; Xie *et al*., 2017; Zhao *et al*., 2018) and antihyperglycemic effects (Yusoff, Yam, Beh *et al*., 2015).

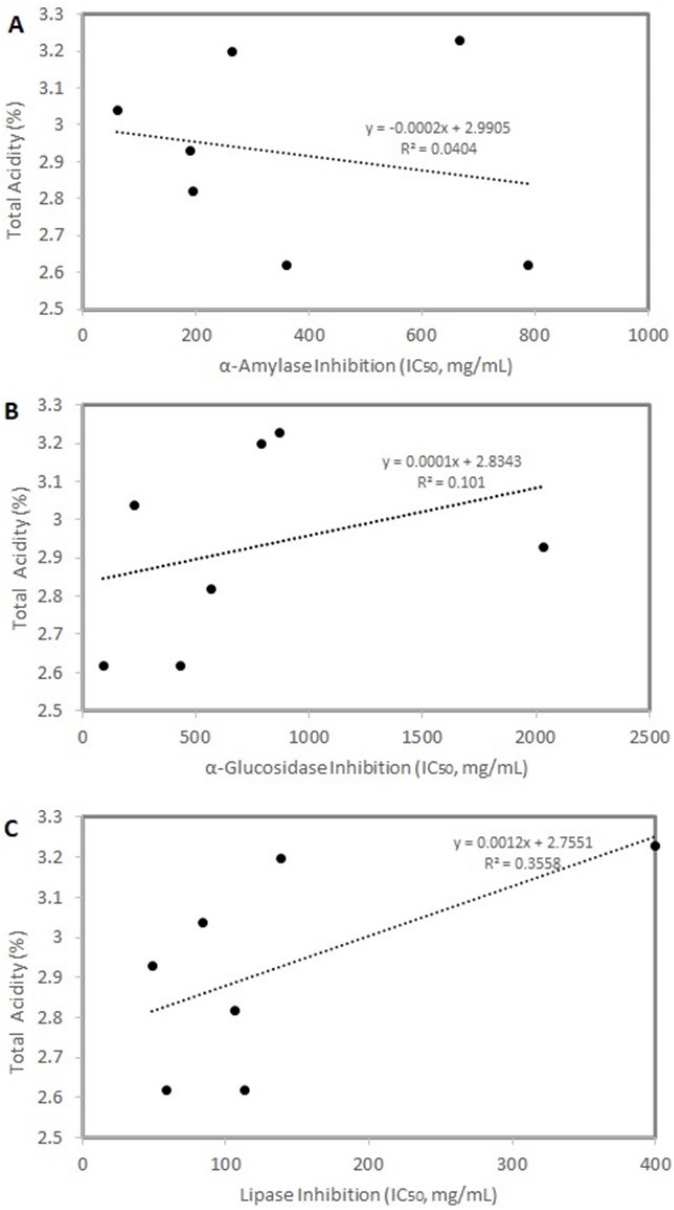

Figure 3. Relationship between the percentage of total acidity with (A) α-amylase, (B) α-glucosidase and (C) lipase inhibitory activities

4. Conclusion

The results presented here and those from previous studies suggest that vinegar have favourable effects in both healthy individuals and Type 2 diabetic patients. Vinegar can be incorporated into the diet to lower the meal's glycemic index and benefit those at risk of diabetes as well as diabetics.

Conflict of interest

The authors declare that there is no conflict of interest.

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References

Abdullah, A., Peeters, A., de Courten, M. and Stoelwinder, J. (2010). The magnitude of association between overweight and obesity and the risk of diabetes: a meta-analysis of prospective cohort studies. *Diabetes Research and Clinical Practice*, 89 (3), 309-319. https://doi.org/10.1016/j.diabres.2010.04.012

Bakir, S., Devecioglu, D., Kayacan, S., Toydemir, G., Karbancioglu-Guler, F. and Capanoglu, E. (2017).

Investigating the antioxidant and antimicrobial activities of different vinegar. *European Food Research and Technology*, 243(12), 2083-2094. https://doi.org/10.1007/s00217-017-2908-0

Chatatikun, M. and Kwanhian, W. (2020). Phenolic Profile of Nipa Palm Vinegar and Evaluation of Its Antilipidemic Activities. *Evidence-Based Complementary and Alternative Medicine,* 2020. https://doi.org/10.1155/2020/6769726

Chen, J.C., Zheng, B.D., Zhao, Y.Y., Xu, J., Wu, J.J. and Luo, C., Pang, J. and He, G.Q. (2012). Hypolipidemic effects on lipid metabolism and lipase inhibition by black vinegar powder. *Journal of Biobased Materials and Bioenergy*, 6(6), 634-639. https://doi.org/10.1166/jbmb.2012.1307

Chen, J., Tian, J., Ge, H., Liu, R. and Xiao, J. (2017). Effects of tetramethylpyrazine from Chinese black vinegar on antioxidant and hypolipidemia activities in hepg2 cells. *Food and Chemical Toxicology,* 109, 930-940. https://doi.org/10.1016/j.fct.2016.12.017

Dechakhamphu, A. and Wongchum, N. (2015). Screening for anti-pancreatic lipase properties of 28 traditional Thai medicinal herbs. *Asian Pacific Journal of Tropical Biomedicine,* 5(12), 1042-1045. https://doi.org/10.1016/j.apjtb.2015.09.012

Feng, Y., Lu, F., Wu, X., Li, Y., Shen, Y., Fan, L., He, Z. and Gao, K. (2015). Inhibitory potential of phenylpropanoid glycosides from *ligustrum purpurascens* kudingcha against α-glucosidase and α -amylase *in vitro*. *International Journal of Food Science and Technology,* 50(10), 2280-2289. https://doi.org/10.1111/ijfs.12887

Halima, B.H., Sarra, K., Houda, B. J., Sonia, G. and Abdallah, A. (2016). Antihyperglycemic, antihyperlipidemic and modulatory effects of apple cider vinegar on digestive enzymes in experimental diabetic rats. *International Journal of Pharmacology,* 12(5), 505-513. https://doi.org/10.3923/ijp.2016.505.513

International Diabetes Federation (IDF). (2019). IDF Diabetes Atlas, 9th Edition. Retrieved on September 30, 2020 from IDF Website: www.diabetesatlas.org/en/resources/.

Jo, Y.H., Kim, S.B., Liu, Q., Do, S.-G., Hwang, B.Y. and Lee, M.K. (2017). Comparison of pancreatic lipase inhibitory isoflavonoids from unripe and ripe fruits of *Cudrania tricuspidata*. *PloS One,* 12(3), e0172069. https://doi.org/10.1371/journal.pone.0172069

Johnston, C.S., Quagliano, S. and White, S. (2013). Vinegar ingestion at mealtime reduced fasting blood glucose concentrations in healthy adults at risk for type 2 diabetes. *Journal of Functional Foods,* 5(4), 2007-2011. https://doi.org/10.1016/j.jff.2013.08.003

Johnston, C.S., Steplewska, I., Long, C.A., Harris, L.N. and Ryals, R.H. (2010). Examination of the antiglycemic properties of vinegar in healthy adults. *Annals of Nutrition and Metabolism,* 56(1), 74-79. https://doi.org/10.1159/000272133

Kan, L., Capuano, E., Fogliano, V., Oliviero, T. and Verkerk, R. (2020). Tea polyphenols as a strategy to control starch digestion in bread: the effects of polyphenol type and gluten. *Food and Function,* 11 (7), 5933-5943. https://doi.org/10.1039/D0FO01145B

Kelebek, H., Kadiroğlu, P., Demircan, N.B. and Selli, S. (2017). Screening of bioactive components in grape and apple vinegar: Antioxidant and antimicrobial potential. *Journal of the Institute of Brewing,* 123(3), 407-416. https://doi.org/10.1002/jib.432

Kwon, Y.I., Apostolidis, E. and Shetty, K. (2008). Inhibitory potential of wine and tea against α-Amylase and α-Glucosidase for management of hyperglycemia linked to type 2 diabetes. *Journal of Food Biochemistry,* 32(1), 15-31. https://doi.org/10.1111/j.1745-4514.2007.00165.x

Liatis, S., Grammatikou, S., Poulia, K.A., Perrea, D., Makrilakis, K., Diakoumopoulou, E. and Katsilambros, N. (2010). Vinegar reduces postprandial hyperglycaemia in patients with type II diabetes when added to a high, but not to a low, glycaemic index meal. *European Journal of Clinical Nutrition,* 64(7), 727-732. https://doi.org/10.1038/ejcn.2010.89

Liu, T.T., Liu, X.T., Chen, Q.X. and Shi, Y. (2020). Lipase inhibitors for obesity: A review. *Biomedicine and Pharmacotherapy,* 128, 110314. https://doi.org/10.1016/j.biopha.2020.110314

Moon, Y.J., Choi, D.S., Oh, S.H., Song, Y.S. and Cha, Y.S. (2010). Effects of persimmon vinegar on lipid and carnitine profiles in mice. *Food Science and Biotechnology,* 19(2), 343-348. https://doi.org/10.1007/s10068-010-0049-3

Ogawa, N., Satsu, H., Watanabe, H., Fukaya, M., Tsukamoto, Y., Miyamoto, Y. and Shimizu, M. (2000). Acetic acid suppresses the increase in disaccharidase activity that occurs during culture of caco-2 cells. *The Journal of Nutrition,* 130(3), 507-513. https://doi.org/10.1093/jn/130.3.507

Petsiou, E.I., Mitrou, P.I., Raptis, S.A. and Dimitriadis, G.D. (2014). Effect and mechanisms of action of vinegar on glucose metabolism, lipid profile, and body weight. *Nutrition Reviews,* 72(10), 651-661. https://doi.org/10.1111/nure.12125

Safamansouri, H., Nikan, M., Amin, G., Sarkhail, P., Gohari, A.R., Kurepaz-Mahmoodabadi, M. and Saeidnia, S. (2014). α-Amylase inhibitory activity of some traditionally used medicinal species of Labiatae. *Journal of Diabetes and Metabolic Disorders,* 13, 114. https://doi.org/10.1186/s40200-014-0114-1

Samad, A., Azlan, A. and Ismail, A. (2016). Therapeutic effects of vinegar: A review. *Current Opinion in Food Science,* 8, 56-61. https://doi.org/10.1016/j.cofs.2016.03.001

Schnurr, T.M., Jakupović, H., Carrasquilla, G.D., Ängquist, L., Grarup, N., Sørensen, T.I., Tjønneland, A.Overvad, K.Pedersen, O.Hansen, T. and Kilpeläinen, T.O. (2020). Obesity, unfavourable lifestyle and genetic risk of type 2 diabetes: a case-cohort study. *Diabetologia*, 63, 1324 - 1332. . https://doi.org/10.1007/s00125-020-05140-5

Seo, H., Jeon, B.-D. and Ryu, S. (2015). Persimmon vinegar ripening with the mountain-cultivated ginseng ingestion reduces blood lipids and lowers inflammatory cytokines in obese adolescents. *Journal of Exercise Nutrition and biochemistry,* 19 (1), 1-10. https://doi.org/10.5717/jenb.2015.19.1.1

Sperling, M.A., Tamborlane, W.V., Battelino, T., Weinzimer, S.A. and Phillip, M. (2014). *Chapter - 19 Diabetes Mellitus* (4th ed.). Philadelphia, PA: Elsevier Saunders. https://doi.org/10.1016/B978-1-4557-4858-7.00028-7

Venkatakrishnan, K., Chiu, H.F. and Wang, C.K. (2019). Extensive review of popular functional foods and nutraceuticals against obesity and its related complications with a special focus on randomized clinical trials. *Food and Function,* 10(5), 2313-2329. https://doi.org/10.1039/C9FO00293F

Wasai, M., Fujimura, Y., Nonaka, H., Kitamura, R., Murata, M. and Tachibana, H. (2018). Postprandial glycaemia-lowering effect of a green tea cultivar Sunrouge and cultivar-specific metabolic profiling for determining bioactivity-related ingredients. *Scientific Reports,* 8(1), 1-9. https://doi.org/10.1038/s41598-018-34316-8

Xia, T., Zhang, B., Duan, W., Zhang, J. and Wang, M. (2020). Nutrients and bioactive components from vinegar: A fermented and functional food. *Journal of Functional Foods,* 64, 103681. https://doi.org/10.1016/j.jff.2019.103681

Xie, X., Zheng, Y., Liu, X., Cheng, C., Zhang, X., Xia, T., Yu, S. and Wang, M. (2017). Antioxidant activity of Chinese Shanxi aged vinegar and its correlation with polyphenols and flavonoids during the brewing process. *Journal of Food Science,* 82(10), 2479-2486. https://doi.org/10.1111/1750-3841.13914

Yamashita, H. (2016). Biological function of acetic acid–improvement in obesity and glucose tolerance by acetic acid in type 2 diabetic rats. *Critical Reviews in Food Science and Nutrition,* 56(Sup1), S171-S175. https://doi.org/10.1080/10408398.2015.1045966

Yusoff, N.A., Ahmad, M., Al Hindi, B., Widyawati, T., Yam, M.F., Mahmud, R., Razak, K.N.A. and Asmawi, M.Z. (2015). Aqueous extract of *Nypa fruticans* Wurmb. vinegar alleviates postprandial hyperglycemia in normoglycemic rats. *Nutrients,* 7 (8), 7012-7026. https://doi.org/10.3390/nu7085320

Yusoff, N.A., Yam, M.F., Beh, H.K., Razak, K.N.A., Widyawati, T., Mahmud, R., Ahmad, M. and Asmawi, M.Z. (2015). Antidiabetic and antioxidant activities of *Nypa fruticans* Wurmb. vinegar sample from Malaysia. *Asian Pacific Journal of Tropical Medicine,* 8(8), 595-605. https://doi.org/10.1016/j.apjtm.2015.07.015

Zhao, C., Xia, T., Du, P., Duan, W., Zhang, B., Zhang, J., Zhu, S. Zheng, Y. Wang, M. and Yu, Y. (2018). Chemical composition and antioxidant characteristic of traditional and industrial Zhenjiang aromatic vinegar during the aging process. *Molecules,* 23(11), 2949. https://doi.org/10.3390/molecules23112949

